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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,689	06/29/2007	Ryan Smith Westberry	186257/US	9609
28381 7590 05/18/2010 ARNOLD & PORTER LLP ATTN: IP DOCKETING DEPT. 555 TWELFTH STREET, N.W. WASHINGTON, DC 20004-1206				
EXAMINER KIM, YOUNG J				
ART UNIT 1637		PAPER NUMBER		
NOTIFICATION DATE 05/18/2010		DELIVERY MODE ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IP.Docketing@aporter.com

Office Action Summary

Application No.

10/588,689

Applicant(s)

WESTBERRY ET AL.

Examiner

Young J. Kim

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13, 14, 19-21, 24-30 and 32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13, 14, 19-21, 24-30 and 32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The present Office Action is responsive to the Amendment received on March 4, 2010.

Preliminary Remark

Claims 12, 14, 15-18, 22, 23, and 31 are canceled.

Claim 32 is new.

Claim Duplication Warning

The claim duplication warning for claims 31, 2-10, 20, and 21 under 37 CFR 1.75 as being a substantial duplicates of claims 1-10, 20, and 21, made in the Office Action mailed on September 29, 2009 is withdrawn in view of the Amendment received on March 4, 2010.

The claim duplication warning for claims 12, and 22-30 under 37 CFR 1.75 as being a substantial duplicate thereof claims 11, 13, 19, and 24-30, made in the Office Action mailed on September 29, 2009 is withdrawn in view of the Amendment received on March 3, 2010.

Claim Rejections - 35 USC § 112

The rejection of claims 1-14 and 19-31 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on September 29, 2009 is withdrawn in view of the Amendment received on March 3, 2010.

Rejection, New Grounds – Necessitated by Amendment

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 13, 14, 19-21, 24-30, and 32 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 11 are indefinite for reciting the phrase, "in an amount generally equivalent to the concentrations of ..." because it is unclear what amount is deemed "generally" equivalent. As no proper metes and bounds can be established for such an amount, the claims are indefinite.

Claims 2-10, 13, 14, 19-21, 24-30, and 32 are indefinite by way of their dependency on claim 1 or 11.

Claim Rejections - 35 USC § 102

The rejection of claims 12 and 31 under 35 U.S.C. 102(b) as being anticipated by Bohlander, S.K. (U.S. Patent No. 5,731,171, issued March 24, 1998), made in the Office Action mailed on September 29, 2009 is withdrawn in view of the Amendment received on March 3, 2010, canceling the rejected claims.

The rejection of claims 11, 12, 24, 25, and 27-31 under 35 U.S.C. 102(a) and (e) as being anticipated by Mukai et al. (US 2003/0073081 A1, published April 17, 2003, filed August 23, 2001) made in the Office Action mailed on September 29, 2009 is withdrawn in view of the Amendment received on March 3, 2010. Specifically, Mukai et al. teaches that their method is used with the presence of UDG or UNG to which the instant claims explicitly exclude.

Rejection, Maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 2, 3, 7-11, 24, 25, and 27-30 under 35 U.S.C. 102(b) as being anticipated by Bohlander, S.K. (U.S. Patent No. 5,731,171, issued March 24, 1998), made in the Office Action mailed on September 29, 2009 is maintained for the reasons already of record.

Applicants' arguments presented in the Amendment received on March 3, 2010 have been fully considered but they are not found persuasive for the reasons set forth in the, "Response to Arguments" section.

The Rejection:

Bohlander discloses a reagent composition comprising:

each of dATP, dCTP, dGTP, and dTTP ("following conditions: ... 150 uM each dATP, dGTP, and dCTP, 110 uM dTTP...") in combination with dUTP ("... 40 uM Bio-11-dUTP..."), wherein said dUTP is at about 10 to 50% of dTTP ($40/110 = 37\%$ of dTTP is dUTP), wherein said mixture comprises a fluorescent probe, beacon or intercalating dye ("products may also be labeled with the fluorophore Spectrum-Orange" column 20, lines 59-63), thereby anticipating claim 1.

Bohlander detects the amplified product (see column 24, lines 33-36, hybridization against cDNA libraries on solid support).

With regard to claims 2 and 3, the artisans also contemplate a mixture comprising 150 uM of each dNTPs and 30 uM of dUTP, which translates to the presence of dUTP at 20% of dTTP concentration.

With regard to claims 7 and 8, the concentration of dUTP (40 uM or 30 uM) does not exceed 300 or 100 uM.

With regard to claims 9 and 10, the artisans disclose that the composition comprises a polymerase (Taq DNA polymerase, see column 20, lines 50-54), and a buffer system (Tris HCl).

Therefore, Bohlander anticipates the invention as claimed.

Response to Arguments:

Applicants traverse the rejection (Page 6, 1st paragraph, Reponse).

Applicants state that Bohlander discloses a reagent composition comprising a “Bio-11-dUTP.” (page 6, 1st paragraph, Response).

Applicants contend that because Bohlander discloses a conjugated dUTP the disclosed mixture is different from the instant claims which require dUTPs (page 6, Response, 2nd paragraph, Response).

This argument is not found persuasive.

It is respectfully submitted that generic recitation of dUTPs cover all species therein, including but not limited to conjugated dUTPs. Consider for example, an independent claim 1 drawn to a composition comprising dUTP. Then consider a dependent claim which depend from said independent claim which recites, “the composition of claim 1, wherein said dUTP is a Bio-11-dUTP.” Would this dependent claim be a proper dependent claim? Obviously, the answer to that question would be a “yes,” since the generic recitation of the term, “dUTP” embraces all subspecies therein, including but not limited to conjugated dUTPs such as Bio-11-dUTP.

Applicants then contend that Bohlander only uses these dUTP functionalized with a detectable label, e.g., Bio-11 or Spectrum-Orange while the present invention employs dUTPs for the purpose of reducing primer aggregation (page 6, 2nd paragraph, Response).

This argument has been carefully considered, but is not found persuasive.

Consider the breadth of Applicants’ claims. It covers any and all range of dATP, dGTP, dCTP and dTTP and dUTP mixture, so long as the dTTP to dUTP ratio is between 9:1 to 1:1. Such a large breadth of the claim potentially reads on any reactions for RT-PCR which would requires a

mixture of dATP, dGTP, dCTP, dTTP, and dUTP, wherein the concentration would conceivably be embraced by the breadth of the instant claims, notwithstanding the fact that their concentration is not intended for reducing primer aggregation. In addition, one would question if Applicants were also even in possession of a reasonable number of species of mixtures of all possible dNTP concentrations which are capable of reducing primer aggregation so as to justify such a large genus.

Consequently, the intended usage of the claim for the presently claimed "product" claim, has not been given any patentable weight. In addition, even if one were to give it patentable weight, if the product of the prior art is substantially same to that of the claimed product, the burden falls on the Applicants to prove that the product of the prior art is different from the product of the claims.

Next, Applicants state that the claims have been amended so that a uracil-degrading enzyme is not present in the reaction mixture (Page 6, 3rd paragraph, Response).

This argument, however, does not appear to apply to Bohlander since Applicants produce no citation of where Bohlander actually discloses that UNG UDG should be used.¹

With regard to Applicants' arguments directed to an "isothermal amplification reaction," this argument is moot because the argument made in reference to the rejection of Mukai, not Bohlander.

The rejection is proper and thus maintained herein.

Claims 1-3, 5, and 7-10 under 35 U.S.C. 102(a) and (e) as being anticipated by Mukai et al. (US 2003/0073081 A1, published April 17, 2003, filed August 23, 2001), made in the Office Action mailed on September 29, 2009 is maintained for the reasons already of record.

¹ This argument appears to apply to the rejection over Mukai.

Applicants' arguments presented in the Amendment received on March 3, 2010 have been fully considered but they are not found persuasive for the reasons set forth in the, "Response to Arguments" section.

The Rejection:

Mukai et al. disclose a reaction mixture for primer-based amplification, said reaction mixture comprising:

each conventional nucleotide dATP, dCTP, dGTP, and dTTP in combination with dUTP as a replacement for a portion of the dTTP ("A reaction mixture of total volume of 0.625 mM each of dATP, dCTP, and dGTP, 0.625 mM of a dTTP+Aminoallyl dUTP mixture" (section [0955]), wherein said dUTP replaces from about 10 to about 50% of said dTTP in said reaction mixture ("The ratio of amino group introduced into an ICAN amplification product was examined by changing the ratio of the amount of dTTP to the amount of Aminoallyl dUTP in the ICAN reaction as follows: 10:0, 9:1, **8:2, 7:3 and 6:4**." section [0954]); and

at least one of a fluorescent probe, beacon or intercalating dye ("After electrophoresis [of the amplified product], fluorescent dye was detected using FM-BIO. Furthermore, the ICAN-amplified fragment was detected by staining with EtBr." section [0958]), thereby clearly anticipating claims 1-3.

The artisans teach a method of amplifying and detecting the amplified product ("After electrophoresis [of the amplified product], fluorescent dye was detected using FM-BIO. Furthermore, the ICAN-amplified fragment was detected by staining with EtBr." section [0958])

² dTTP/dUTP ratio of 8:2, 7:3, and 6:4, necessarily means that 20 % of what would be dTTP (to be 100% dTTP) is dUTP. Similarly, the ratio of 7:3 would necessarily mean 30% of what would be dTTP would be dUTP; and the ratio of 6:4 would necessarily mean 40% of what would be dTTP would be dUTP.

With regard to claim 5, the artisans employ a primer pair, SEQ ID Numbers 281 and 282, which are chimeric primers comprising a combination of ribonucleotides and deoxyribonucleotides (section [0955] and “SEQ ID NO: 281:—Designed chimeric oligonucleotide primer designated as MF2N3(24). ‘nucleotides 22 to 24 are ribonucleotides-other nucleotides are deoxyribonucleotides.’”; “SEQ ID NO: 282: Designed chimeric oligonucleotide primer designated as MR1N3(24). ‘nucleotides 22 to 24 are ribonucleotides-other nucleotides are deoxyribonucleotides.’” sections [1250] and [1251]).

With regard to claims 7 and 8, the artisans disclose that the concentration of dNTPs used is 0.625 mM, and thus, dUTP concentration would not exceed about 300 uM or about 100 uM (since 9:1 ratio of dTTP:dUTP in the amount of 0.625 mM (or 625 uM) would be 62.5 uM).

With regard to claims 9, and 10, the reagent mixture disclosed by the artisans comprises HEPES-potassium hydroxide buffer and BcaBEST DNA polymerase (section [0955]).

Therefore, Mukai et al. clearly anticipate the invention as claimed.

Response to Arguments:

Applicants traverse the rejection (Page 6, 1st paragraph, Reponse).

Applicants state that Mukai discloses a reagent composition comprising a “Aminoallyl-dUTP.” (page 6, 1st paragraph, Response).

Applicants contend that because Mukai discloses a conjugated dUTP the disclosed mixture is different from the instant claims which require dUTPs (page 6, Response, 2nd paragraph, Response).

This argument is not found persuasive.

It is respectfully submitted that generic recitation of dUTPs cover all species therein, including but not limited to conjugated dUTPs. Consider for example, an independent claim 1 drawn to a composition comprising dUTP. Then consider a dependent claim which depend from

said independent claim which recites, "the composition of claim 1, wherein said dUTP is a Bio-11-dUTP." Would this dependent claim be a proper dependent claim? Obviously, the answer to that question would be a "yes," since the generic recitation of the term, "dUTP" embraces all subspecies therein, including but not limited to conjugated dUTPs such as Aminoallyl-dUTP.

Applicants contend that the present invention employs dUTPs for the purpose of reducing primer aggregation (page 6, 2nd paragraph, Response).

This argument has been carefully considered, but is not found persuasive.

Consider the breadth of Applicants' claims. It covers any and all range of dATP, dGTP, dCTP and dTTP and dUTP mixture, so long as the dTTP to dUTP ratio is between 9:1 to 1:1. Such a large breadth of the claim potentially reads on any reactions for RT-PCR which would require a mixture of dATP, dGTP, dCTP, dTTP, and dUTP, wherein the concentration would conceivably be embraced by the breadth of the instant claims, notwithstanding the fact that their concentration is not intended for reducing primer aggregation. In addition, one would question if Applicants were also even in possession of a reasonable number of species of mixtures of all possible dNTP concentrations which are capable of reducing primer aggregation so as to justify such a large genus.

Consequently, the intended usage of the claim for the presently claimed "product" claim, has not been given any patentable weight. In addition, even if one were to give it patentable weight, if the product of the prior art is substantially same to that of the claimed product, the burden falls on the Applicants to prove that the product of the prior art is different from the product of the claims.

Next, Applicants state that the claims have been amended so that a uracil-degrading enzyme is not present in the reaction mixture (Page 6, 3rd paragraph, Response).

This argument is not found persuasive since the mixture at point prior to the addition of UDG or UNG would still anticipate the mixture of the claimed invention.

With regard to Applicants' arguments directed to an "isothermal amplification reaction," this argument is moot because the presently rejected claims are drawn to a product and thus, the intended usage has no bearing on the differences between the prior art product and the product of the instant invention.

The rejection is proper and thus maintained herein.

Claim Rejections - 35 USC § 103

The rejection of claims 13, 14, 19-23, and 26 under 35 U.S.C. 103(a) as being unpatentable over Mukai et al. (US 2003/0073081 A1, published April 17, 2003, filed August 23, 2001) in view of McLaughlin et al. (U.S. Patent No. 6,783,940 B2, issued August 31, 2004, filed October 31, 2001; cited previously), made in the Office Action mailed on September 29, 2009 is withdrawn in view of the Amendment received on March 4, 2010. Specifically, Mukai et al. teaches that their method is used with the presence of UDG or UNG to which the instant claims explicitly exclude and McLaughlin et al. do not cure this deficiency.

Rejection, Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 4 and 6 under 35 U.S.C. 103(a) as being unpatentable over Mukai et al. (US 2003/0073081 A1, published April 17, 2003, filed August 23, 2001) in view of McLaughlin et al. (U.S. Patent No. 6,783,940 B2, issued August 31, 2004, filed October 31, 2001; cited previously),

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made in the Office Action mailed on September 29, 2009 is maintained for the reasons already of record.

Applicants' arguments presented in the Amendment received on March 4, 2010 have been fully considered but they are not found persuasive for the reasons set forth in the, "Response to Arguments" section.

The Rejection:

The teachings of Mukai et al. have been discussed above.

Mukai et al. do not disclose the use of mannitol or sorbitol.

McLaughlin et al. disclose that sorbitol reduces non-specific amplification in a DNA polymerase chain reaction involving sorbitol (column 2, lines 13-15), with said sorbitol concentration ranging from 0.25M to 0.35M (which is 250 mM to 350 mM, respectively; column 2, lines 25-27).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Mukai et al. with the teachings of McLaughlin et al., thereby arriving at the claimed invention for the following reasons.

As Mukai et al. demonstrate a method of amplifying a target nucleic acid sequence using PCR primers, said one of ordinary skill in the art would have been reasonably motivated to employ other reagent means which would also further aid in specific target amplification, such as that of McLaughlin et al.

In *KSR International Co. v. Teleflex Inc.* (KSR), (citation omitted), the Supreme Court expressed that, "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *Id.* at ___, 82 USPQ2d at 1395.

Clearly, one of ordinary skill in the art at the time the invention was made would have recognized that adding art-recognized amounts of sorbitol in an amplification reaction mixture, as evidenced by McLaughlin et al., would have resulted in the predictable result of providing higher specificity in amplification reaction.

Additionally, the MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success.

To this end, McLaughlin state the following:

"Other dNTPs, such as deoxyuridine triphosphate ("dUTP"), and dNTP analogs [which would be considered to be non-conventional nucleotides], and conjugated dNTPs may also be used..." (column 6, lines 19-22; McLaughlin et al.)

"Deoxynucleotide triphosphates ("dNTPs"), which are the building blocks of the amplification nucleic acid molecules, are typically supplied in standard PCR reactions at a concentration of 40-200 μ M each ..." (column 6, lines 14-17) with contemplation of, "higher than 200 μ M..." being advantageous (column 6, lines 25-26; McLaughlin et al.)

Provided that McLaughlin et al. explicitly state that the reagents employed by Mukai et al. (dNTPs including dUTPs in PCR reactions) are combinable and workable at the same ranges (40-200 μ M each, and higher than 200 μ M), one of ordinary skill in the art would have had no doubt that the combination of the teaching would have been successful.

As to the primers, wherein all the thymidines are completely replaced by uracil, such modification would have been obvious to one of ordinary skill in the art, for the purpose of generating amplicons which comprises all uracil bases in the amplified products.

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Response to Arguments:

Applicants' arguments with respect to the method of use has been duly considered and the rejection was withdrawn. However, with respect to the product claims, all of Applicants' arguments have been addressed and have not been found persuasive. Since no new arguments are presented for this rejection, the rejection is maintained herein.

Rejections, New Grounds – Necessitated by Amendment

Claims 13, 14, 19, 20, 21, 26, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohlander, S.K. (U.S. Patent No. 5,731,171, issued March 24, 1998) in view of McLaughlin et al. (U.S. Patent No. 6,783,940 B2, issued August 31, 2004, filed October 31, 2001; cited previously).

The teachings of Bohlander et al. have already been discussed above.

Bohlander et al. do not teach the use of mannitol or sorbitol.

McLaughlin et al. disclose that sorbitol reduces non-specific amplification in a DNA polymerase chain reaction involving sorbitol (column 2, lines 13-15), with said sorbitol concentration ranging from 0.25M to 0.35M (which is 250 mM to 350 mM, respectively; column 2, lines 25-27).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Bohlander et al. with the teachings of McLaughlin et al., thereby arriving at the claimed invention for the following reasons.

As Bohlander et al. demonstrate a method of amplifying a target nucleic acid sequence using PCR primers, said one of ordinary skill in the art would have been reasonably motivated to employ other reagent means which would also further aid in specific target amplification, such as that of McLaughlin et al.

In *KSR International Co. v. Teleflex Inc.* (*KSR*), (citation omitted), the Supreme Court expressed that, “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *Id.* at ___, 82 USPQ2d at 1395.

Clearly, one of ordinary skill in the art at the time the invention was made would have recognized that adding art-recognized amounts of sorbitol in an amplification reaction mixture, as evidenced by McLaughlin et al., would have resulted in the predictable result of providing higher specificity in amplification reaction.

Additionally, the MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success.

To this end, McLaughlin et al. state the following:

“Other dNTPs, such as deoxyuridine triphosphate (“dUTP”), and dNTP analogs [which would be considered to be non-conventional nucleotides], and conjugated dNTPs may also be used...” (column 6, lines 19-22; McLaughlin et al.)

“Deoxynucleotide triphosphates (“dNTPs”), which are the building blocks of the amplification nucleic acid molecules, are typically supplied in standard PCR reactions at a concentration of 40-200 μ M each ...” (column 6, lines 14-17) with contemplation of, “higher than 200 μ M...” being advantageous (column 6, lines 25-26; McLaughlin et al.)

Provided that McLaughlin et al. explicitly state that the reagents employed by Bohlander et al. (dNTPs including dUTPs in PCR reactions) are combinable and workable at the same ranges (40-200 μ M each, and higher than 200 μ M), one of ordinary skill in the art would have had no doubt that the combination of the teaching would have been successful.

As to the primers, wherein all the thymidines are completely replaced by uracil, such modification would have been obvious to one of ordinary skill in the art, for the purpose of generating amplicons which comprises all uracil bases in the amplified products.

Lastly, with respect to the new claim 32, Bohlander et al. explicitly disclose that their amplification reaction involve a melting temperature of more than about 60°C (column 3, lines 50-51; column 4, lines 5-8).

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 6:00 a.m. to 2:30 p.m (M-F). The Examiner can

also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner
Art Unit 1637
5/14/2010

/YJK/